



**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PV/395/PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/CZ 03/00049	International filing date (day/month/year) 26.08.2003	Priority date (day/month/year) 27.08.2002
International Patent Classification (IPC) or both national classification and IPC C07D495/04		
Applicant ZENTIVA, A.S. et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 4 sheets, including this cover sheet.  
  
☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  
  
 These annexes consist of a total of sheets.

- This report contains indications relating to the following items:
  - I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application

Date of submission of the demand  08.03.2004	Date of completion of this report  18.11.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Schmid, A  Telephone No. +49 89 2399-8591  

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/CZ 03/00049

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-7 as originally filed

**Claims, Numbers**

1-7 as originally filed

**Drawings, Sheets**

1/5-5/5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/CZ 03/00049**

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-6
	No: Claims	7
Inventive step (IS)	Yes: Claims	1-6
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-7
	No: Claims	

2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

---

International application No. PCT/CZ 03/00049

**Re Item V**

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1) US-A-6,429,210 (D1) discloses in figures 1-4 the x-ray and infrared spectra of the form 1 of clopidogrel hydrogen sulfate which has been previously prepared in US-A-4,847,265 (cf. also D1, col. 1, lines 26-38).

The applicant has claimed the form 1 in claim 7 by a product-by-process formulation. However, the characterisation of a product does not render the product novel if it is known per se from the prior art (cf. above).

Accordingly the subject-matter of present claim 7 is not novel with regard Article 33(2) PCT.

- 2) The present preparation method differs from the ones known from D2 and especially D1 in the use of a solvent chosen from lower alcohols and their esters with lower acids whereas D1 precipitates the clopidogrel hydrogen sulfate out of acetone thereby obtaining the thermodynamically stable form II.

Therefore the subject-matter of present claims 1-6 is novel pursuant to Article 33(2) PCT.

Since it was not predictable from D1 that such a change in the process would lead to a reliable method (cf. present examples) of obtaining form I of clopidogrel hydrogen sulfate in a high yield also an inventive step according to Article 33(3) PCT can be acknowledged for present claims 1-6.